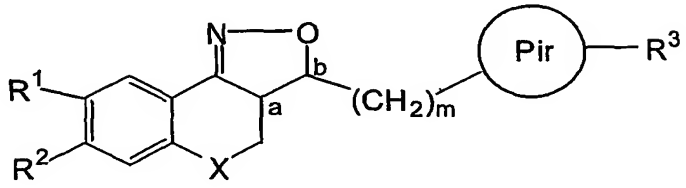
CLAIMS

1. A compound according to the general Formula (I)



(I)

the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof and the *N*-oxide form thereof, wherein:

X is CH_2, N-R^7, S or O ;

R^7 is selected from the group of hydrogen, alkyl, Ar, Ar-alkyl, alkylcarbonyl, alkyloxycarbonyl and mono- and di(alkyl)aminocarbonyl;

R^1 and R^2 are each selected from the group of hydrogen, halo, hydroxy, -OSO_2H, –OSO_2CH_3, alkyloxy, alkyloxyalkyloxy, alkyloxyalkyloxyalkyloxy, tetrahydrofuranyloxy, alkylcarbonyloxy, alkyloxyalkylcarbonyloxy, pyridinylcarbonyloxy, alkylcarbonyloxyalkyloxy, alkyloxycarbonyloxy, alkenyloxy, alkenylcarbonyloxy, mono- or di(alkyl)aminoalkyloxy, –N-$R^{10}R^{11}$, alkylthio, Alk, Ar and Het,

with the proviso that at least one of R^1 and R^2 is selected from the group of Alk, Ar and Het, wherein

Alk is cyano, CN-OH, CN-oxyalkyl, alkyl, alkyloxyalkyl, alkyloxyalkyloxyalkyl, alkyloxyalkyloxyalkyloxyalkyl, alkylcarbonylalkyl, alkylcarbonyloxyalkyl, alkyloxycarbonylalkyl, Ar-alkyl, Ar-carbonylalkyl, Ar-oxyalkyl, mono- or di(alkyl)aminoalkyl, mono- or di(alkylcarbonyl)aminoalkyl, mono- or di(alkyl)amino-carbonylalkyl, Het-alkyl, formyl, alkylcarbonyl, alkyloxycarbonyl, alkyloxyalkylcarbonyl, mono- or di(alkyl)aminocarbonyl, Ar-carbonyl and Ar-oxycarbonyl ;

Ar is phenyl or naphthyl, optionally substituted with one or more halo, cyano, oxo, hydroxy, alkyl, formyl, alkyloxy or amino radicals.

Het is a heterocyclic radical selected from the group of Het^1, Het^2 and Het^3 ;

Het^1 is an aliphatic monocyclic heterocyclic radical selected from the group of pyrrolidinyl, dioxolyl, imidazolidinyl, pyrrazolidinyl, piperidinyl,

dioxyl, morpholinyl, dithianyl, thiomorpholinyl, piperazinyl and tetrahydrofuryl ;

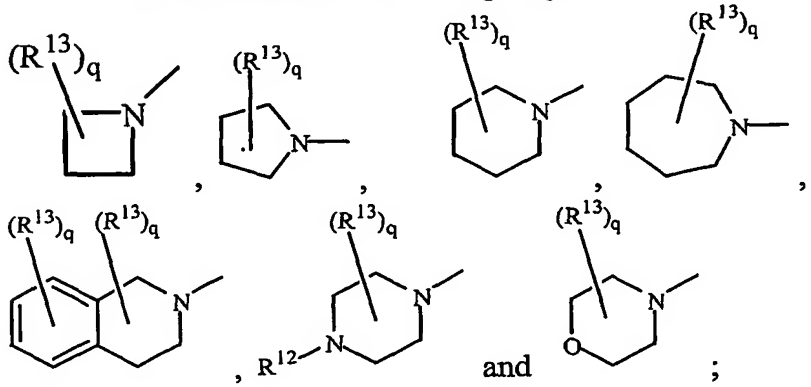
Het^2 is a semi-aromatic monocyclic heterocyclic radical selected from the group of 2H-pyrrolyl, pyrrolinyl, imidazolinyl and pyrrazolinyl ;

Het^3 is an aromatic monocyclic heterocyclic radical selected from the group of pyrrolyl, pyrazolyl, imidazolyl, furyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl and triazinyl; or an aromatic bicyclic heterocyclic radical selected from the group of quinolinyl, quinoxalinyl, indolyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzisothiazolyl, benzofuranyl and benzothienyl ;

wherein each Het^1, Het^2 and Het^3-radical may optionally be substituted on either a carbon or heteroatom with halo, hydroxy, alkyloxy, alkyl, Ar, Ar-alkyl, formyl, alkylcarbonyl or pyridinyl ;

R^{10} and R^{11} are each, independently from each other, selected from the group of hydrogen, alkyl, Ar, Ar-alkyl, pyrrolidinylalkyl, piperidinylalkyl, homopiperidinylalkyl, piperazinylalkyl, morpholinylalkyl, mono- or di(alkyl)aminoalkyl, alkylcarbonyl, alkenylcarbonyl, Ar-carbonyl, pyridinylcarbonyl, alkyloxycarbonyl, mono- or di(alkyl)aminocarbonyl, mono- or di(Ar)aminocarbonyl, mono- or di(alkyloxycarbonylalkyl)-aminocarbonyl, pyrrolidinylcarbonyl, aminoiminomethyl, alkylaminoiminomethyl, *N*-benzylpiperazinyliminomethyl, alkylsulphonyl and Ar-sulphonyl ; or

R^{10} and R^{11} may be taken together and with the N may form a monovalent radical selected from the group of



wherein :

R^{12} is selected from the group of hydrogen, alkyl, Ar, Ar-alkyl,

Ar-alkenyl, alkylcarbonyl, alkyloxycarbonyl, alkyloxyalkylcarbonyl and mono- or di(alkyl)aminocarbonyl ;

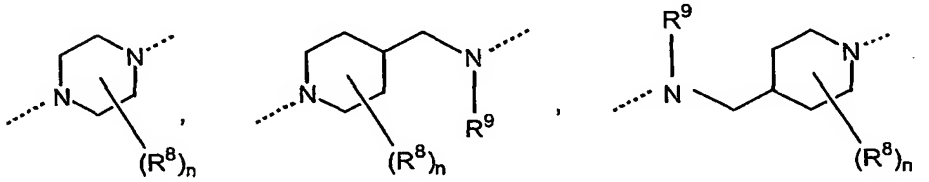
each ring being optionally substituted with q radicals R^{13}, each radical independently from each other selected from the group of alkyl, oxo, Ar, Ar-alkyl, Ar-alkenyl and alkyloxycarbonyl and q being an integer ranging from 0 to 6 ; or

R^1 and R^2 may be taken together to form a bivalent radical $-R^1-R^2-$ selected from the group of $-CH_2-CH_2-CH_2-CH_2-$, $-CH=CH-CH_2-CH_2-$, $-CH_2-CH_2-CH=CH-$, $-CH_2-CH=CH-CH_2-$ and $-CH=CH-CH=CH$;

a and b are asymmetric centers ;

$(CH_2)_m$ is a straight hydrocarbon chain of m carbon atoms, m being an integer ranging from 1 to 4 ;

Pir is a radical according to any one of Formula (IIa), (IIb) or (IIc)



(II)

(a) (b) (c)

optionally substituted with n radicals R^8, wherein :

each R^8 is independently from each other, selected from the group of hydroxy, amino, nitro, cyano, halo and alkyl ;

n is an integer ranging from 0 to 5 ;

R^9 is selected from the group of hydrogen, alkyl and formyl;

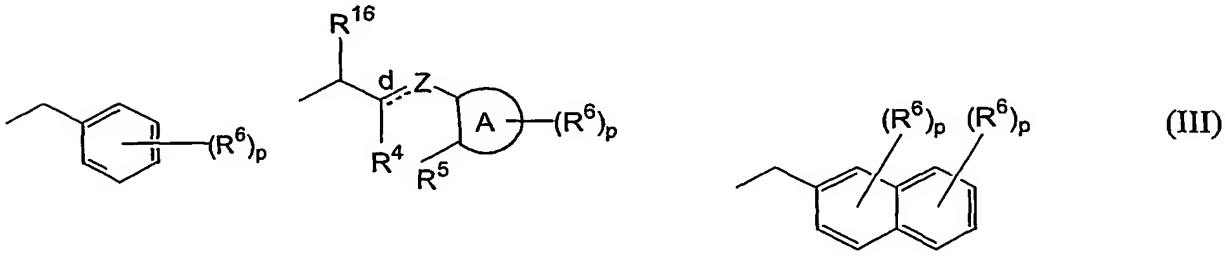
R^3 represents an optionally substituted aromatic homocyclic or heterocyclic ring system together with an optionally substituted and partially or completely hydrogenated hydrocarbon chain of 1 to 6 atoms long with which said ring system is attached to the Pir radical and of which may contain one or more heteroatoms selected from the group of O, N and S ;

alkyl represents a straight or branched saturated hydrocarbon radical having from 1 to 6 carbon atoms or a cyclic saturated hydrocarbon radical having from 3 to 6 carbon atoms, optionally substituted with one or more halo, cyano, oxo, hydroxy, formyl or amino radicals ;

alkenyl represents a straight or branched unsatured hydrocarbon radical having one or more double bonds, optionally substituted with one or more halo, cyano, oxo, hydroxy, formyl or amino radicals ; and

halo is fluoro, chloro, bromo and iodo.

2 A compound according to claim 1, characterized in that R^3 is a radical according to any one of Formula (IIIa), (IIIb) or (IIIc)



(III)

(a) (b) (c)

wherein :

d is a single bond while Z is a bivalent radical selected from the group of $-CH_2-$, -C(=O)-, -CH(OH)-, -C(=N-OH)-, –CH(alkyl)-, -O-, -S-, -S(=O)-, -NH- and –SH-; or d is a double bond while Z is a trivalent radical of formula =CH- or =C(alkyl)- ;

A is a 5- or 6-membered aromatic homocyclic or heterocyclic ring, selected from the group of phenyl, pyranyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, thienyl, isothiazolyl, pyrrolyl, imidazolyl, pyrazolyl, furanyl, oxadiazolyl and isoxazolyl ;

p is an integer ranging from 0 to 6 ;

R^4 and R^5 are each, independently from each other, selected from the group of hydrogen, alkyl, Ar, biphenyl, halo and cyano ; or

R^4 and R^5 may be taken together to form a bivalent radical $-R^4-R^5-$ selected from the group of $-CH_2-$, =CH-, $-CH_2-CH_2-$, -CH=CH- , -O-, -NH-, =N-, -S-, $-CH_2N(-alkyl)-$, $-N(-alkyl)CH_2-$, $-CH_2NH-$, $-NHCH_2-$, -CH=N-, -N=CH-, $-CH_2O-$ and $-OCH_2-$;

each R^6 is independently from each other, selected from the group of hydroxy, amino, nitro, cyano, halo, carboxyl, alkyl, Ar, alkyloxy, Ar-oxy, alkylcarbonyloxy, alkyloxycarbonyl, alkylthio, mono- and di(alkyl)amino, alkylcarbonylamino, mono- and

di(alkyl)aminocarbonyl, mono- and di(alkyl)aminocarbonyloxy, mono- and di(alkyl)aminoalkyloxy ; or

two vicinal radicals R^6 may be taken together to form a bivalent radical $-R^6-R^6-$ selected from the group of $-CH_2-CH_2-O-$, $-O-CH_2-CH_2-$, $-O-CH_2-C(=O)-$, $-C(=O)-CH_2-O-$, $-O-CH_2-O-$, $-CH_2-O-CH_2-$, $-O-CH_2-CH_2-O-$, $-CH=CH-CH=CH-$, $-CH=CH-CH=N-$, $-CH=CH-N=CH-$, $-CH=N-CH=CH-$, $-N=CH-CH=CH-$, $-CH_2-CH_2-CH_2-$, $-CH_2-CH_2-C(=O)-$, $-C(=O)-CH_2-CH_2-$, $-CH_2-C(=O)-CH_2-$ and $-CH_2-CH_2-CH_2-CH_2-$ and

R^{16} is selected from the group of hydrogen, alkyl, Ar and Ar-alkyl.

3. A compound according to claim 2, characterized in that X=O ; m = 1 ; Pir is a radical according to Formula (IIa) wherein n =0 ; R^3 is a radical according to Formula (IIIb) wherein d is a double bond while Z is a trivalent radical of formula =CH-, A is a phenyl ring, R^4 is hydrogen or alkyl, R^5 and R^{16} are each hydrogen, R^6 is hydrogen or halo and p = 1.

4. A compound according to any one of claims 1 to 3, characterized in that at least one of R^1 and R^2 is selected from the group of cyano optionally substituted with hydroxy or alkyloxy ; alkyl ; hydroxyalkyl ; aminoalkyl ; alkyloxyalkyl ; alkyloxyalkyloxyalkyloxyalkyl ; alkylcarbonyloxyalkyl ; Ar-oxyalkyl ; mono- or di(alkyl)aminoalkyl, the alkyl radicals optionally substituted with hydroxy ; mono- or di(alkylcarbonyl)aminoalkyl ; mono- or di(alkyl)aminocarbonyl ; piperidinylalkyl ; morpholinylalkyl ; phenyl and thienyl optionally substituted with alkylcarbonyl.

5. A compound according to any one of claims 1 to 4 with the following name:

- 8-Methyl-3-[4-(3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole (compound 1) ;
- 8-Methoxy-7-methyl-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole (compound 2);
- {8-Methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazol-7-yl}-methanol (compound 4);
- 7-Methoxymethyl-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole (compound 5);
- 8-Methoxy-7-(2-methoxy-ethoxymethoxymethyl)-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole (compound 6) ;

- Acetic acid 8-methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazol-7-ylmethyl ester (compound 7) ;
- 8-Methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-7-phenoxymethyl-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole (compound 8) ;
- 2-(Methyl-{3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazol-7-ylmethyl}-amino)-ethanol (compound 9) ;
- 8-Methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-7-morpholin-4-ylmethyl-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole (compound 10);
- 3-[4-(2-Methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole-7-carbaldehyde oxime (compound11);
- 3-[4-(2-Methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole-7-carbaldehyde O-methyl-oxime (compound 12);
- 3-[4-(2-Methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole-7-carbonitrile (compound 13);
- *N*-{3-[4-(2-Methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazol-7-ylmethyl}-acetamide (compound 15) ;
- 8-Methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole-7-carboxylic acid ethylamide (compound 16) ;
- 8-Methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-7-phenyl-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazole (compound 17) ;
- 1-(5-{8-Methoxy-3-[4-(2-methyl-3-phenyl-allyl)-piperazin-1-ylmethyl]-3a,4-dihydro-*3H*-chromeno[4,3-c]isoxazol-7-yl}-thiophen-2-yl)-ethanone (compound 18).

6. A compound which is degraded *in vivo* to yield a compound according to any one of claims 1 to 5.

7. A compound according to any one of claims 1 to 6 for use as a medicine.

8. The use of a compound according to any one of claims 1 to 7 for the manufacture of a medicament for the treatment and/or prophylaxis of depression, anxiety, movement disorders, psychosis, Parkinson's disease and body weight disorders.

9. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredient a therapeutically effective amount of a compound according to any one of claims 1 to 7.

10. A process for making a pharmaceutical composition according to claim 9, comprising mixing a compound according to any one of claims 1 to7 and a pharmaceutically acceptable carrier.

11. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredient a therapeutically effective amount of a compound according to any one of claims 1to 7 and one or more other compounds selected from the group of antidepressants, anxiolytics and antipsychotics and anti-Parkinson's disease drugs .

12. The use of a pharmaceutical composition according to claim 11 for the manufacture of a medicament to improve efficacy and/or onset of action in the treatment and/or prophylaxis of depression, anxiety, movement disorders, psychosis, Parkinson's disease and body weight disorders.

13. The use of a compound according to any one of claims 1 to 7 for the manufacture of a medicament for the treatment and/or prophylaxis of depression, anxiety, movement disorders, psychosis, Parkinson's disease and body weight disorders, said treatment comprising the simultaneous or sequential administration of a compound according to any one of claims 1-7 and one or more other compounds selected from the group of antidepressants, anxiolytics, anti-psychosis and anti-Parkinson's drugs.

14. The use of one or more compounds selected from the group of antidepressants, anxiolytics and antipsychotics for the manufacture of a medicament for the treatment and/or prophylaxis of depression, anxiety and body weight disorders, said treatment comprising the simultaneous or sequential administration of one or more compounds selected from the group of antidepressants, anxiolytics and antipsychotics and anti-Parkinson's disease drugs and a compound according to any one of claims 1 to 7.

15. The use of a pharmaceutical composition according to claim 11 to improve

efficacy and/or onset of action in the treatment and/or prophylaxis of depression, anxiety, movement disorders, psychosis, Parkinson's disease and body weight disorders.

16. A process for making a pharmaceutical composition according to claim 11, comprising mixing a compound according to any one of claims 1 to 7 and a compound selected from the group of antidepressants, anxiolytics, antipsychotics and anti-Parkinson's disease drugs and a pharmaceutically acceptable carrier.